

## AMENDMENTS TO THE CLAIMS:

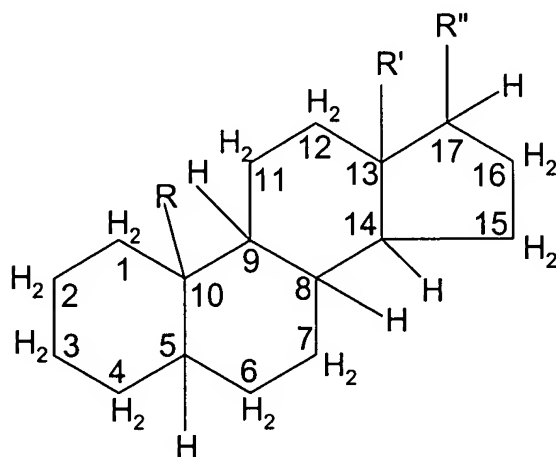
Please amend Claims 1 – 26 as follows:

1. (Original) Nitrooxy derivatives of steroidal compounds of general formula



or esters or salts thereof, wherein:

B is a steroidal radical having the following structure:

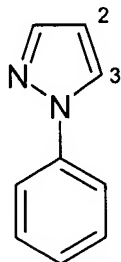


(IA)

wherein at the place of the hydrogen of the CH group, or of the two hydrogens of the CH<sub>2</sub> group indicated in the general formula, there can be the following substituents:

in position 1-2: a double bond;

in position 2-3 the following substituent:



(IA-1);

in position 2: Cl, Br;

in position 3: oxo, -O-CH<sub>2</sub>-CH<sub>2</sub>-Cl, OH, OCH<sub>3</sub>;

in position 4-5: a double bond;

in position 5-6: a double bond;

in position 6: Cl, F, Br, CH<sub>3</sub>, -CHO;

the ring defined by the carbon atoms numbered 1, 2, 3, 4, 5, and 10 is an aromatic ring when B is the residue of an estrogen;

in position 7: Cl, OH;

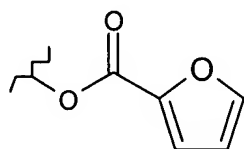
in position 9: Cl, F, Br;

in position 11: OH, oxo, Cl;

in position 16: CH<sub>3</sub>, OH, =CH<sub>2</sub>;

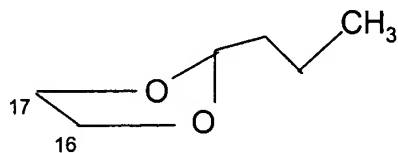
in position 17: OH, CH<sub>3</sub>, OCO(O)<sub>ua</sub>(CH<sub>2</sub>)<sub>va</sub>CH<sub>3</sub> wherein ua is an integer equal to 0 or 1, va is an integer from 0 to 4, ethynyl (C≡CH);

or

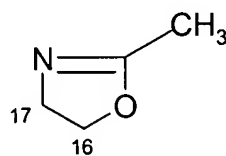


(IA-2)

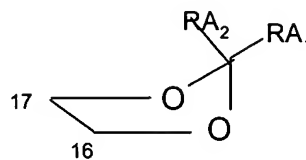
in position 16-17 the following groups:



(IA-3)



(IA-4)



(IA-5)

wherein RA<sub>1</sub> is H, CH<sub>3</sub>; RA<sub>2</sub> is C<sub>1</sub>-C<sub>10</sub> linear or branched alkyl chain, preferably C<sub>1</sub>-C<sub>3</sub>, still more preferably CH<sub>3</sub>, or a saturated cycloaliphatic ring having 5-6 carbon atoms or an aromatic ring optionally substituted in para position with N(R<sub>1c</sub>)<sub>2</sub> wherein R<sub>1c</sub> is a C<sub>1</sub>-C<sub>10</sub>, preferably C<sub>1</sub>-C<sub>4</sub>, linear or branched alkyl; R and

R', equal to or different from each other, can be hydrogen or C<sub>1</sub>-C<sub>4</sub> linear or branched alkyls, preferably R = R' = CH<sub>3</sub> or R = R' = H;

preferably B is a corticosteroid residue;

R" in position 17 is a bivalent radical having one of the following meanings:

IB)  $-(CO-L)_t-(X_O)_{t1}-$ , wherein t = 1 and t<sub>1</sub> is 0 or 1, preferably 0;

IC)  $-L-(X_O)_{t1}-$ , wherein t<sub>1</sub> is 0 or 1, preferably 1;

the bivalent linking group L has the following meaning:



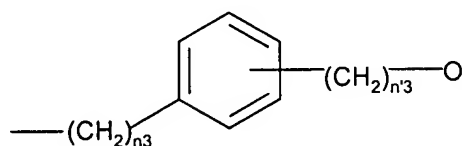
wherein n<sub>a</sub>, n'<sub>a</sub>, and n''<sub>a</sub>, equal to or different from each other, are integers from 0 to 6, preferably 1-3; n<sub>b</sub>, n'<sub>b</sub>, n''<sub>b</sub> and n'''<sub>b</sub>, equal to or different from each other, are integers equal to 0 or 1; R<sub>4</sub>, R<sub>5</sub>, R<sub>4'</sub>, R<sub>5'</sub>, R<sub>4''</sub>, R<sub>5''</sub>, equal to or different from each other, are selected from H, C<sub>1</sub>-C<sub>5</sub>, preferably C<sub>1</sub>-C<sub>3</sub>, linear or branched alkyl;

X<sub>0</sub> = -O-, -NH-, -NR<sub>1c</sub>- wherein R<sub>1c</sub> is as above defined;

the bond between the steroid and the linking group X<sub>1</sub> is of ester or amidic type;

X<sub>1</sub> is a bivalent linking group selected from the following:

- Y<sub>AR1</sub> :

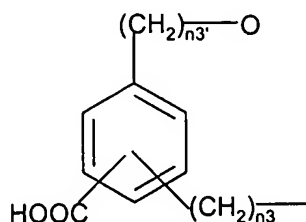


(V)

wherein n<sub>3</sub> is an integer from 0 to 5 and n'<sub>3</sub> is an integer from 1 to

3;

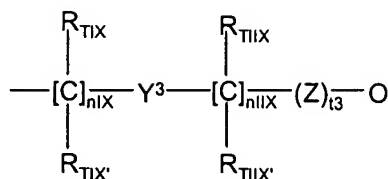
- Y<sub>AR2</sub> :



(VI)

wherein n3 and n3' have the above meaning.

- Y<sub>p</sub>:



(III)

wherein:

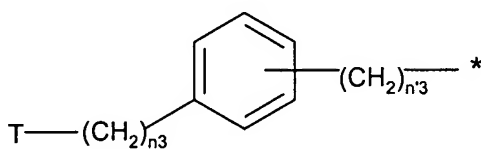
nIX is an integer from 0 to 10, preferably 1-3;

nIIX is an integer from 1 to 10, preferably 1-5;

R<sub>TIX</sub>, R<sub>TIX'</sub>, R<sub>TII</sub>, R<sub>TII'</sub>, equal to or different from each other are H or C<sub>1</sub>-C<sub>4</sub> linear or branched alkyl; preferably R<sub>TIX</sub>, R<sub>TIX'</sub>, R<sub>TII</sub>, R<sub>TII'</sub> are H;  
Y<sup>3</sup> is a saturated, unsaturated or aromatic heterocyclic ring, having 5 or 6 atoms, containing from one to three heteroatoms, preferably from one to two, said heteroatoms being equal or different and selected from nitrogen, oxygen, sulphur, preferably nitrogen;

t3 is zero or 1;

Z has the following meaning:



(VI)

wherein:

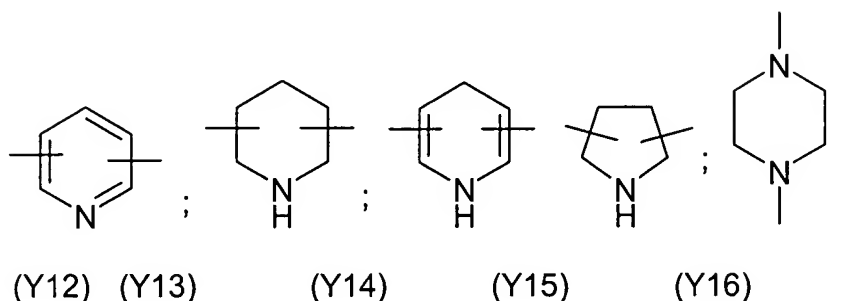
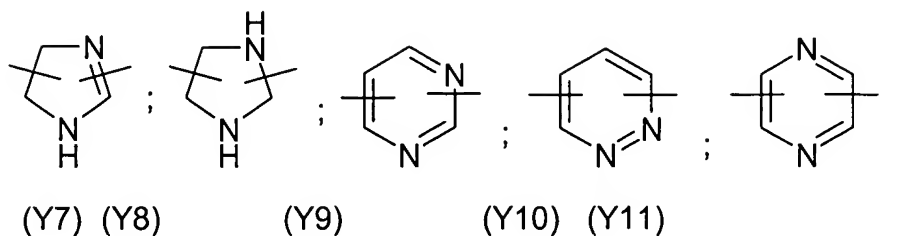
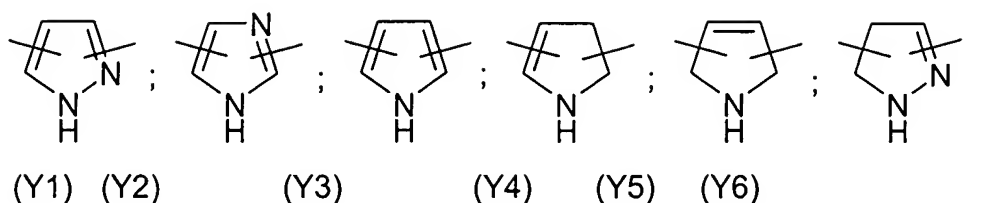
\* shows the position of the ONO<sub>2</sub> group;

T has the following meanings:

- -COX<sub>3</sub>-, -X<sub>3</sub>CO-, wherein X<sub>3</sub> = S or X<sub>o</sub> as above defined;
- -X<sub>3</sub>- as above defined;

n3 and n'3 are as above defined.

2. (Original) Compounds according to claim 1, wherein Y<sup>3</sup> is selected from the following bivalent radicals:



3. (Original) Compounds according to claim 2, wherein  $Y^3$  is selected from the following: (Y12), having the two free valences in the ortho positions with respect to the nitrogen atom; (Y16) with the two valences linked to the two heteroatoms, (Y1) (pyrazol) 3,5-disubstituted; (Y16) is particularly preferred.

4. (Currently Amended) Compounds according to ~~claims 1-3~~ claim 1, wherein the precursor of B is selected from the following: Budesonide, Hy-drocortisone, Alclomethasone, Algestone, Beclomethasone, Betamethasone, Chloroprednisone, Ciclesonide, Clobetasol, Clobetasone, Clcortolone, Cloprednol, Cortisone, Corticosterone, Deflazacort, Desonide, Desoximethasone, Dexamethasone, Dexamethasone 17-furoate, Diflorasone Diflu-cortolone, Difluprednate, Fluazacort, Flucoronide, Flumethasone, Flunisolide, Fluocinolone Acetonide, Fluocinonide, Fluocortyn Butyl, Fluocortolone, Fluorometholone, Fluperolone Acetate, Fluprednidene Acetate, Fluprednisolone, Flurandrenolide, Formocortal, Halcinonide, Halobetasol Propionate, Halomethasone, Halopredone Ace-tate, Hydrocortamate, Itrocinonide, Loteprednol Eta-bonate, Meclonisone, Medrysone, Meprednisone, Methylprednisolone, Momethasone Furoate, Paramethasone, Prednicarbate, Prednisolone, Prednisolone 25-TECH/252960.1

Diethylaminoacetate, Prednisolone Sodium Phosphate, Prednisone, Prednival, Prednylidene, Rofleponide Rimexolone, Triamcinolone, 21-Acetoxyprogesterone, Cortivazol, Amcinonide, Fluticasone Propionate, MaziPredone, Taucorten, Tixocortol, Triamcinolone Hexacetonide; Ursodesoxycholic acid, Chenodesoxycholic acid; Myatrienediol, Moxestrol, Ethynyl-estradiol, Estradiol, Mestranol; methyl (20R)-6- $\alpha$ , 9 $\alpha$ -difluoro-11 $\beta$ -hydroxy-16 $\alpha$ , 17 $\alpha$  propyl methylene dioxyandrosta-1,4-dien-3-one-17 $\beta$ -carboxylate.

5. (Currently Amended) Compounds according to ~~claims 1-4~~ claim 1, wherein when B is the residue of a corticosteroid,  $R'' = IB$  with  $t = 1$  and  $t_1 = 0$ ; preferably in the formula of the linking group  $L$   $n_a = n_b = n''b = 1$ ;  $n'a = n''b = n'''b = n''a = 0$ ;  $R_4 = R_5 = H$ ; or  $n'b = n''b = 1$  and all the other  $n_a, n_b, n'a, n'''b, n''a$  are equal to zero.

6. (Currently Amended) Compounds according to ~~claims 1-4~~ claim 1, wherein when B is the residue of a biliary acid,  $R'' = IC$  with  $t_1 = 1$ ; preferably in the formula of the linking group  $L$   $n_a = n'b = 1$ ,  $n'a = 2$ ,  $n''b = n'''b = n''a = n_b = 0$ ,  $R_4 = CH_3$ ,  $R_5 = R_{4'} = R_{5'} = H$ .

7. (Currently Amended) Compounds according to ~~claims 1-4~~ claim 1, wherein when B is the residue of an estrogen

-  $R'' = IC$  wherein  $t_1 = 0$  and in the formula of the linking group  $L$   $n_b = n'b = 1$ ;  $n_a = n'a = n''b = n'''b = n''a = 0$ , the other substituent of the carbon atom in position 17 is preferably H or ethynyl, and in position 3 one of the substituents is optionally the  $-R''-X_1-NO_2$  group ( $R''$  as above defined);

or

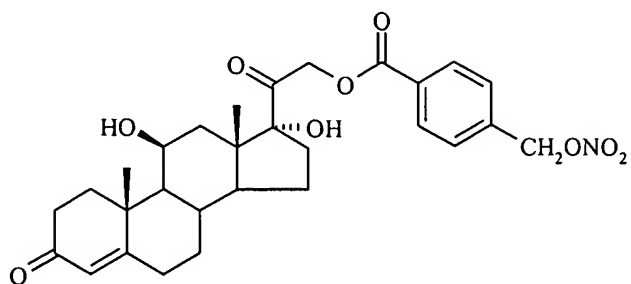
- in position 3 the  $-R''-X_1-NO_2$  group is present,  $R''$  being as above when B is the residue of an estrogen, then the substituents of the carbon atom in position 17 in formula (IA) of B are the following:

-  $R'' = -O-$ , wherein the oxygen free valence is saturated with H;

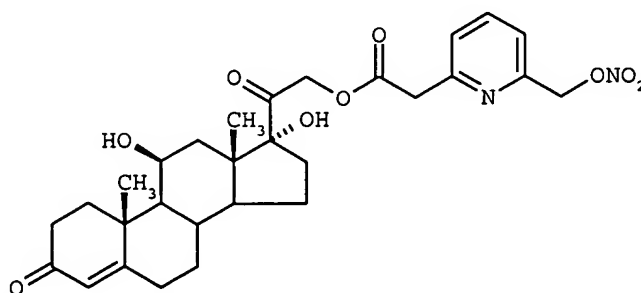
- H is substituted with a group different from OH.

8. (Currently Amended) Compounds according to ~~claims 1-7~~ claim 1,  
selected from the following:

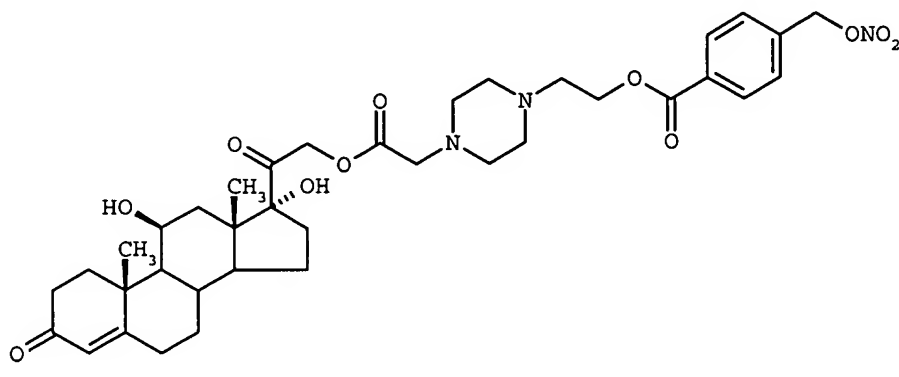
Hydrocortisone 21-(4'-nitrooxymethyl) benzoate



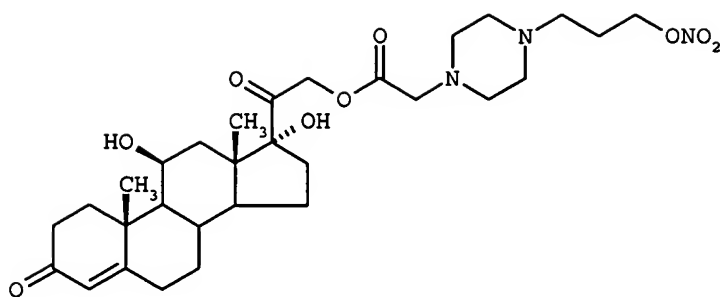
Hydrocortisone-21-[2-[6-(nitrooxymethyl)-2-pyridinyl] acetate]



Hydrocortisone-21[2-[4-[2-[4-(nitrooxymethyl)benzoyloxy] ethyl] 1-piperazinyl]acetate]

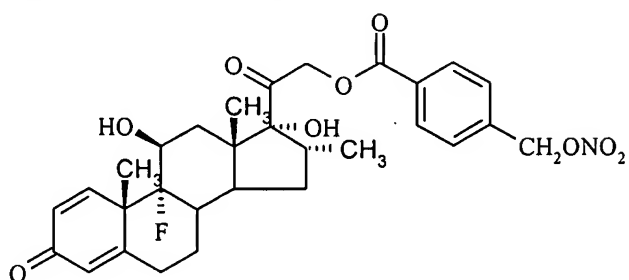


Hydrocortisone-21-[2-[4-[3-(nitrooxy)propyl]-1-pipera-zinyl] acetate]



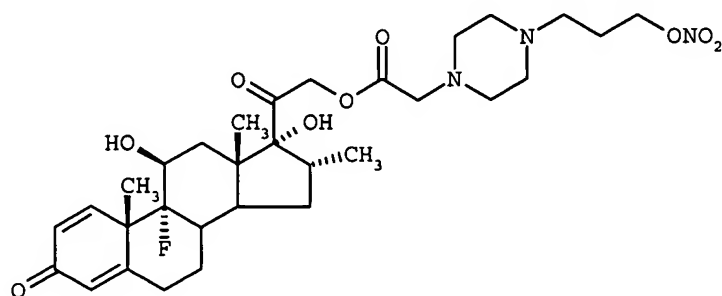
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Dexamethasone 21-(4'-nitrooxymethyl)benzoate



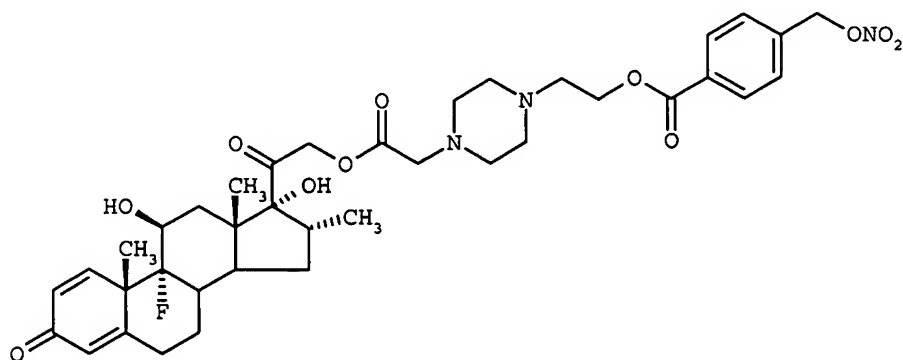
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Dexamethasone-21-[2-[4-[3-(nitrooxy)propyl]-1-piperazinyl] acetate]



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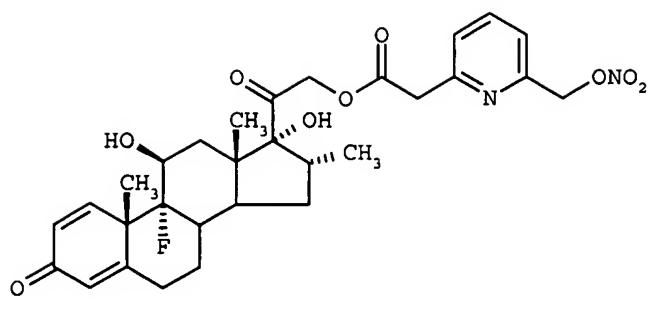
Dexamethasone-21[2-[4-[2-[4-(nitrooxymethyl)benzoyloxy]  
piperazinyl]acetate] ethyl]-1-



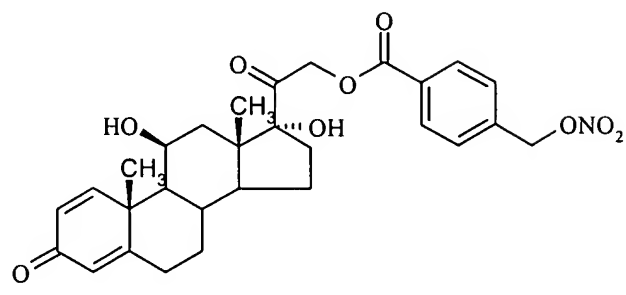
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Dexamethasone-21-[2-[6-(nitrooxymethyl)-2-pyridinyl] acetate]

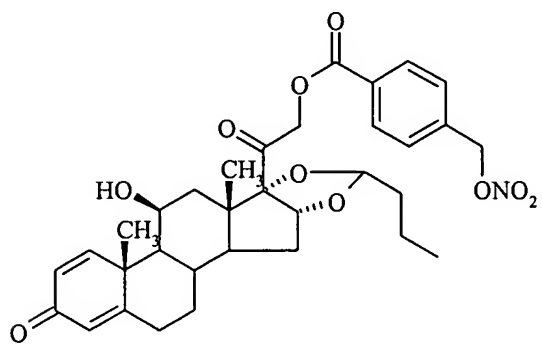




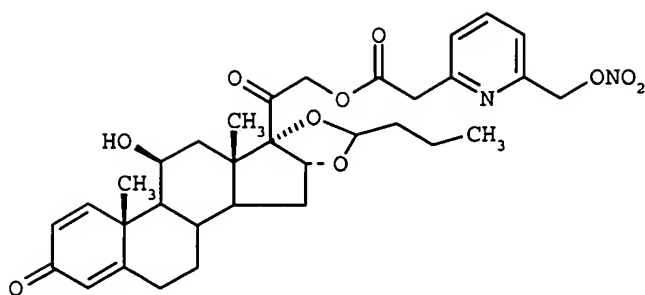
Prednisolone 21-(4'-nitrooxymethyl)benzoate



Budesonide 21-(4'-nitrooxymethyl)benzoate:

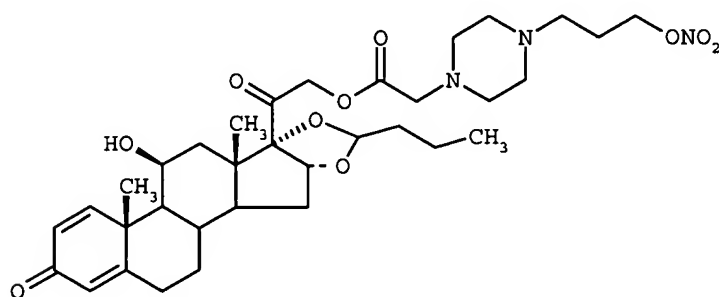


Budesonide-21-[2-[6-(nitrooxymethyl)-2-pyridinyl]acetate]



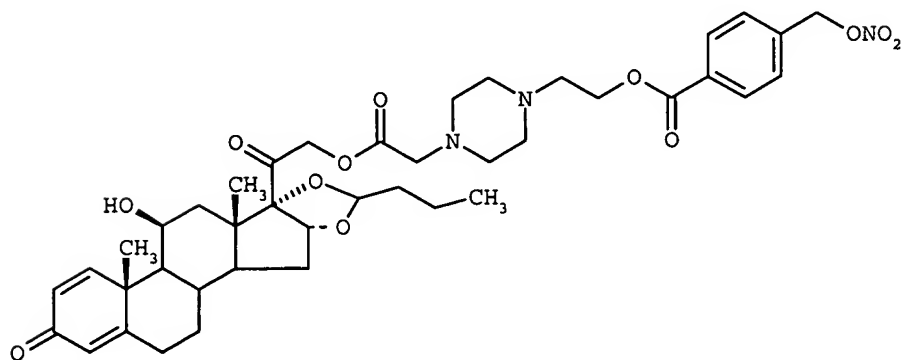
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**Budesonide-21-[2-[4-[3-(nitrooxy)propyl]-1-piperazinyl] acetate]**



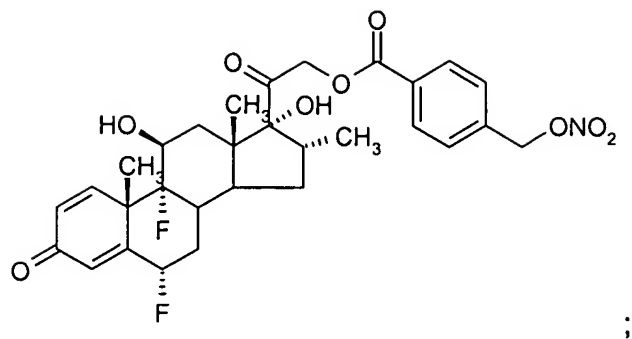
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**Budesonide-21[2-[4-[2-[4-nitrooxymethyl)benzoyl oxy]ethyl]-1-piperazinyl]acetate]**

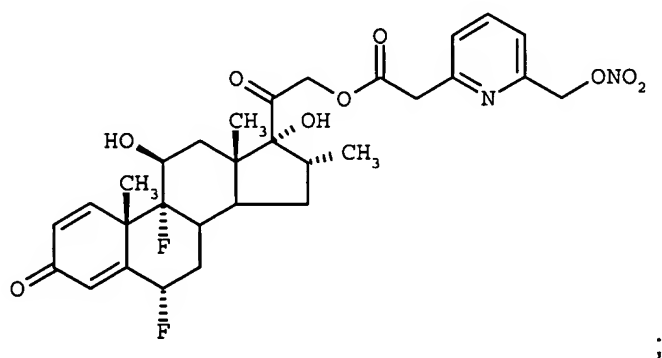


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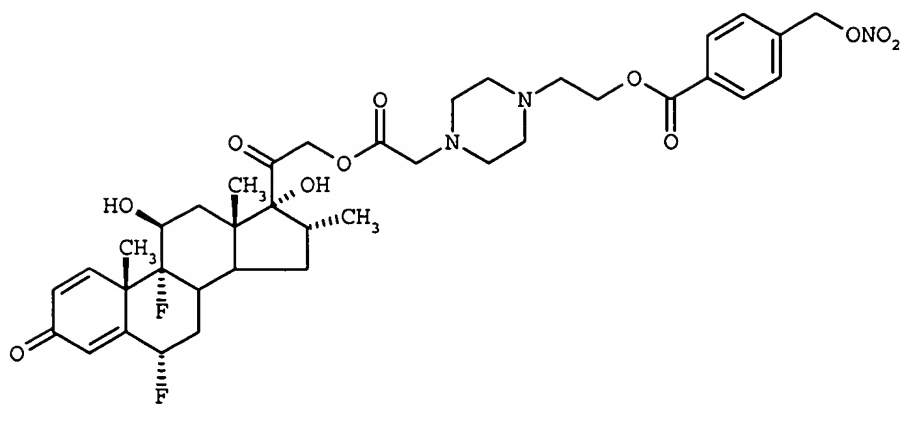
**Flumethasone 21-(4'-nitrooxymethyl)benzoate:**



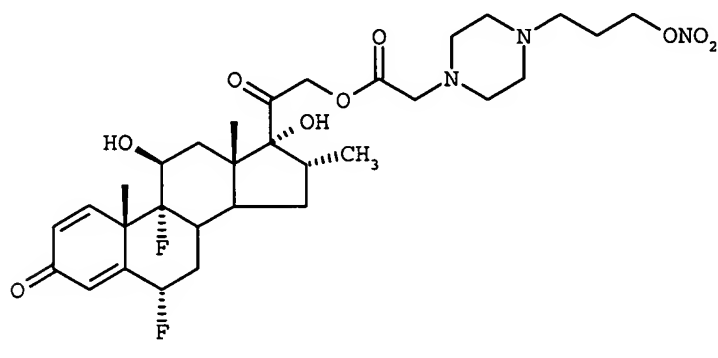
Flumethasone-21-[2-[6-(nitrooxymethyl)-2-pyridinyl]acetate]



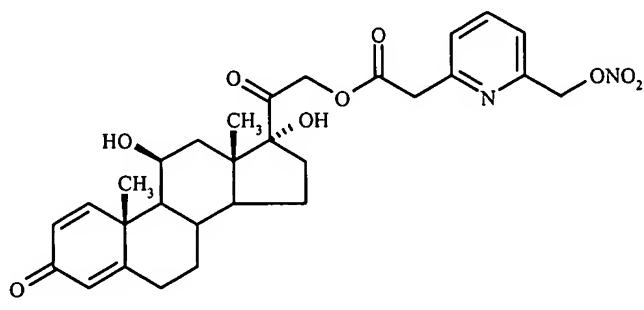
Flumethasone-21[2-[4-[2-[4-(nitrooxymethyl)benzoyloxy]-ethyl]-1-piperazinyl]acetate]



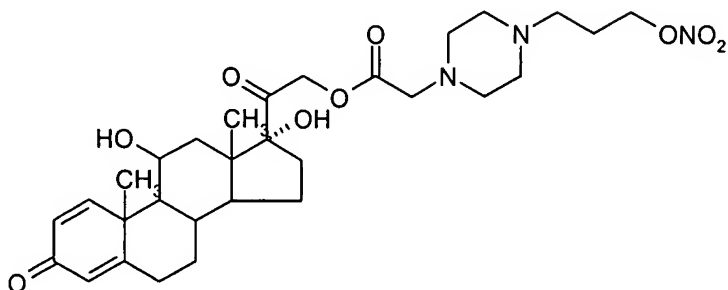
**Flumethasone-21-[2-[4-[3-(nitrooxy)propyl]-1-piperazinyl] acetate]**



**Prednisolone-21-[2-[6-(nitrooxymethyl)-2-pyridinyl] acetate]**

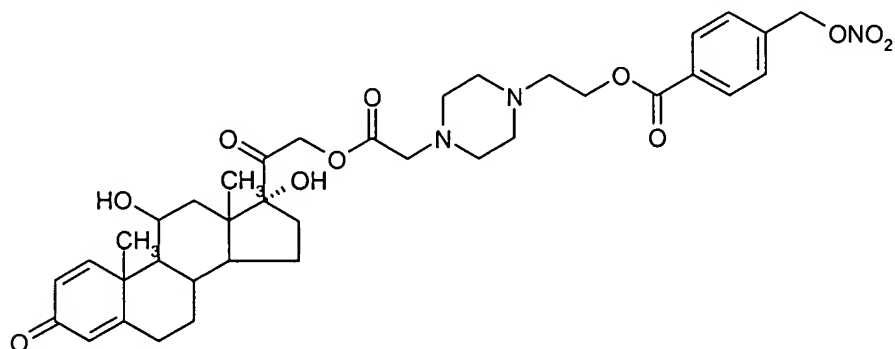


Prednisolone-21-[2-[4-(3-nitrooxy)propyl) piperazin-1-yl] acetate] and the corresponding bishydrochloride salt:



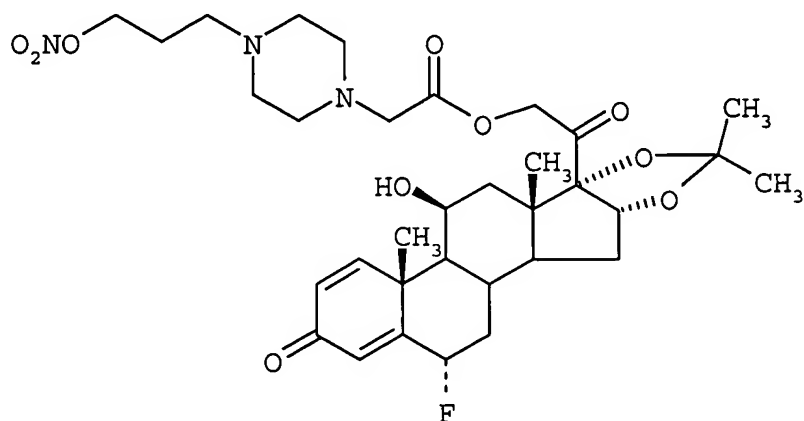
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Prednisolone-21-[2-[4-[2-[(4'-nitrooxymethyl)benzoyl oxy]ethyl]piperazin-1-yl]acetate] and the corresponding bishydrochloride salt:



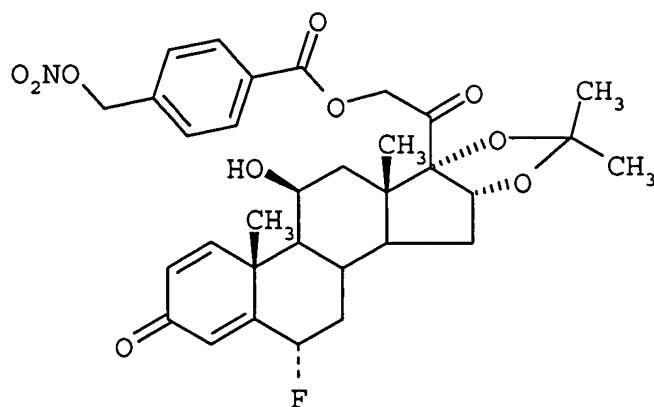
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**Flunisolide-21-[2-[4-[3-(nitrooxy)propyl]-1-piperazinyl] acetate]**



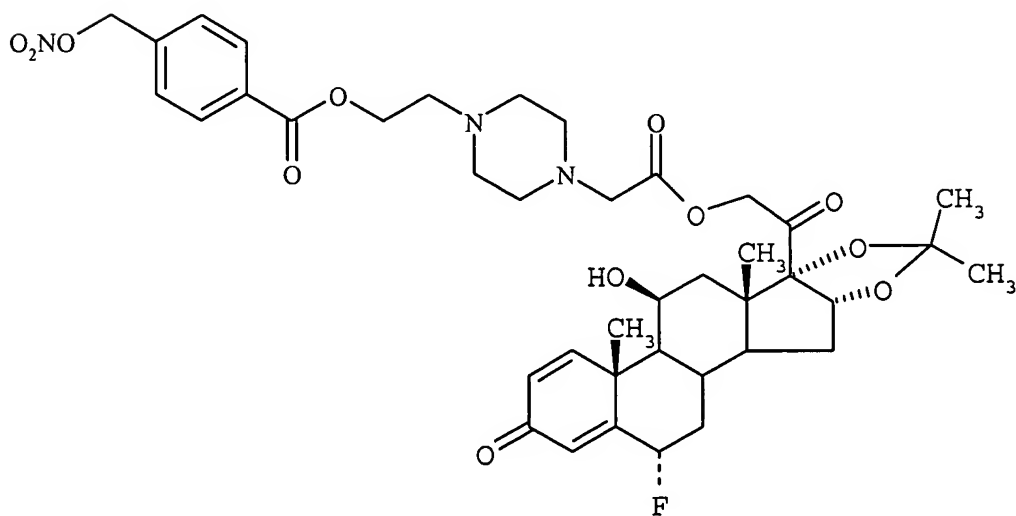
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Flunisolide-21-[(4'-nitrooxymethyl)]benzoate



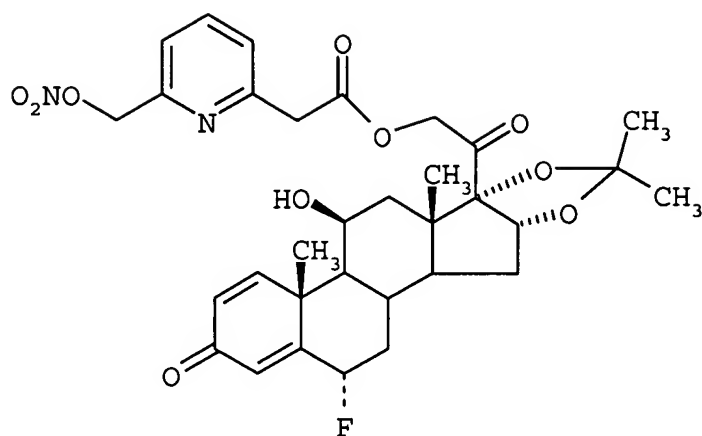
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**Flunisolide-21-[2-[4-[2-[4-(nitrooxymethyl)benzoyloxy] ethyl]-1-piperazinyl]acetate]**

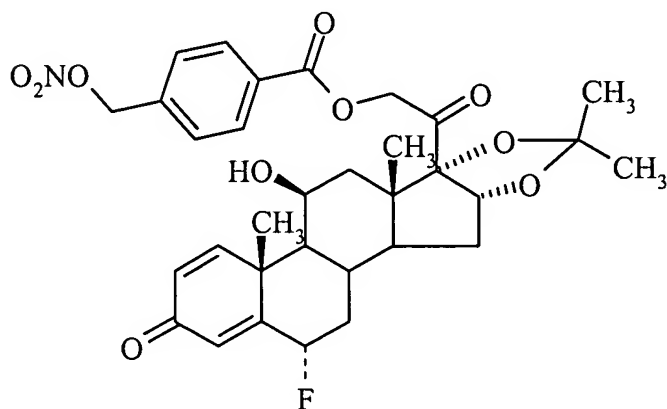


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Flunisolide-21-[2-[6-(nitrooxymethyl)-2-pyridinyl] acetate]



Flunisolide 21-[(4'-nitrooxymethyl)benzoate]]



9. (Currently Amended) Use of the compounds according to ~~claims 1-8~~ claim 1, for the preparation of medicaments.
10. (Currently Amended) Use of the compounds according to ~~claims 1-8~~ claim 1, as drugs having antiinflammatory activity at peripheral level.
11. (Currently Amended) Use of the compounds according to ~~claims 1-8~~ claim 1, for the therapy of neurodegenerative diseases on an inflammatory and traumatic basis of the nervous system.
12. (Currently Amended) Use of the compounds according to ~~claims 1-8~~ claim 1, as drugs having an antiarthritic activity.

13. (Currently Amended) Use of the compounds of ~~claims 1-8~~ claim 1, as drugs having an immunodepressive activity.
14. (Currently Amended) Use of the compounds according to ~~claims 1-8~~ claim 1, as drugs having an angiostatic/angiogenetic activity.
15. (Currently Amended) Use of the compounds according to ~~claims 1-8~~ claim 1, as drugs having an antiasthmatic activity.
16. (Currently Amended) Use of the compounds according to ~~claims 1-8~~ claim 1, in substitutive hormonal therapies, preferably in the post-menopause therapy.
17. (Currently Amended) Use of the compounds according to ~~claims 1-8~~ claim 1, in rheumatic disease therapies.
18. (Currently Amended) Use of the compounds according to ~~claims 1-8~~ claim 1, in renal disease therapies.
19. (Currently Amended) Use of the compounds according to ~~claims 1-8~~ claim 1, in bronchial disease therapies.
20. (Currently Amended) Use of the compounds according to ~~claims 1-8~~ claim 1, in ocular disease therapies.
21. (Currently Amended) Use of the compounds according to ~~claims 1-8~~ claim 1, in dermatologic disease therapies.
22. (Currently Amended) Use of the compounds according to ~~claims 1-8~~ claim 1, in autoimmune disease therapies.
23. (Currently Amended) Use of the compounds according to ~~claims 1-8~~ claim 1, in tumoral process therapies, optionally in combination with chemotherapeutic and/or radiotherapeutic treatments.
24. (Original) Use according to claim 10, in inflammatory pathologies affecting the gastrointestinal system.
25. (Currently Amended) Use of the compounds according to ~~claims 1-8~~ claim 1, wherein the glucocorticoid compounds are used in respiratory pathologies characterized by broncho-obstructive events.
26. (Currently Amended) Pharmaceutical formulations comprising the compounds of ~~claims 1-8~~ claim 1.